

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-18. (cancelled)

19. (new) A molecule comprising three segments :

- a targeting segment C capable of binding to membranes of cells engaged in an apoptosis process ;
- a therapeutic segment A comprising a biologically active compound ; and
- a linker segment L between the targeting segment and the therapeutic segment, said linker segment L being cleavable in vivo in the environment of a tissue or cell undergoing apoptosis.

20. (new) The molecule according to claim 1, wherein said linker segment L comprises a chemical function recognised and cleaved by an enzyme or a set of enzymes specific to the environment of a tissue or of a cell in apoptosis.

21. (new) The molecule according to claim 2, wherein said linker segment L comprises a sequence recognised and cleaved by a protease mainly present in the environment of a tissue or cell undergoing apoptosis, more particularly selected from the group consisting of a metalloprotease of the extracellular matrix, a urokinase, and a

protease specific to cleavage of an extracellular segment of membranous cytokines or of their receptors.

22. (new) The molecule according to claim 1, wherein said linker segment L comprises a sequence selected in that it contains at least one B1-B2 residue couple given in the following table :

B ₁	B ₂
Val/Ala/Leu/Met	X
Leu/Tyr/Phe	X
Ala	Leu
Leu	Val
Val	Cys
Gly	Leu/Ile
Gly	Val
Ala	Val
Asn	Val
Arg	Phe
Gly/Ala/Asn/Glu/Gln/Pro/Arg/His/Asn	Hydrophobic, natural or not
Polar : Arg/Asp/Glu/Gln/Thr/Asn Hydrophobic : Ala	Hydrophobic, natural or not

wherein X is any amino acid residue, natural or not.

23. (new) The molecule according to claim 1, wherein said targeting segment C is capable of binding to membranes comprising lipids having a negative total electrostatic charge, in particular phosphatidylserine.

24. (new) The molecule according to claim 5, wherein said targeting segment comprises the following peptidic sequence :

J¹-J²-J³-J⁴-J⁵-J⁶-Z⁷-U⁸-J⁹-J¹⁰-U¹¹-R-J¹³-J¹⁴-U¹⁵-K-G-X¹⁸-G-T-J²¹-E-J²³-J²⁴-U²⁵-J²⁶-J²⁷-
J²⁸-U²⁹-J³⁰-J³¹-R-J³³-J³⁴-J³⁵-J³⁶-B³⁷-J³⁸-J³⁹-U⁴⁰-J⁴¹-J⁴²-J⁴³-U⁴⁴-J⁴⁵-J⁴⁶-J⁴⁷-J⁴⁸-J⁴⁹-R-J⁵¹-
U⁵²-J⁵³-J⁵⁴-D-U⁵⁶-K-S-Z⁵⁹-L-J⁶¹-J⁶²-J⁶³-J⁶⁴-Z⁶⁵-J⁶⁶-J⁶⁷-U⁶⁸-J⁶⁹-J⁷⁰-J⁷¹-U⁷²-J⁷³-J⁷⁴-J⁷⁵-J⁷⁶

(S1)

wherein J, Z, U, X, and B represent amino acids such that :

- J amino acids are selected, independently of one another, from natural amino acids, or from derivatives thereof, such that at least 50 % of them are polar residues selected from R, N, D, C, Q, E, G, H, K, Orn, P, S, T and Y,

- U amino acids are selected from A, C, G, I, L, M, F, W, Y, and V,

- amino acid X¹⁸ is selected, independently of the other amino acids of the sequence, from A, N, C, Q, G, H, I, L, M, F, S, T, W, Y and V,

- amino acid B³⁷ is selected, independently of the other amino acids of the sequence, from R, A, C, G, I, L, M, F, W, Y, and V,

- amino acid Z⁷ is selected, independently of the other amino acids of the sequence, from D and E,

- amino acids Z⁵⁹ and Z⁶⁵ are selected, independently, from E, D, K, and R,

and wherein exponents indicate the position of the amino acids in the sequence.

25. (new) The molecule according to claim 6, wherein amino acids U and B are selected according to one of the examples given below :

	U ⁸	U ¹¹	U ¹⁵	U ²⁵	U ²⁹	B ³⁷	U ⁴⁰	U ⁴⁴	U ⁵²	U ⁵⁶	U ⁶⁸	U ⁷²
Ex 1	V	L	M	I	L	R	I	Y	L	L	V	L
Ex 2	A	I	I	I	L	R	I	Y	L	L	I	L
Ex 3	A	I	I	I	L	R	I	Y	L	L	M	V
Ex 4	A	L	M	L	L	R	I	Y	L	L	I	M
Ex 5	A	L	M	I	I	R	V	Y	L	L	I	M
Ex 6	A	L	M	I	I	R	I	F	L	L	I	M
Ex 7	A	L	M	I	V	R	I	F	L	L	I	F
Ex 8	V	L	M	I	L	R	I	F	L	L	I	M
Ex 9	A	L	M	I	L	R	I	F	L	L	I	M
Ex10	A	L	M	I	L	R	I	Y	L	L	A	A
Ex11	V	L	M	I	L	R	I	Y	L	L	V	L
Ex12	V	L	M	I	L	R	I	F	L	L	V	L

26. (new) The molecule according to claim 5, wherein said targeting segment C comprises a sequence selected from the group consisting of sequences SEQ ID Nos 23-32.

27. (new) The molecule according to claim 1, wherein said targeting segment C comprises a sequence selected from the group consisting of all or part of an annexin, a C1 or C2 type domain of the blood coagulation factors, a domain V of a protein of the

family of 2-Glycoproteins-I, a FYVE type domain, a PH type domain, and a fragment or a derivative thereof having at least 50 % of identity.

28. (new) The molecule according to claim 9, wherein said targeting segment C comprises a sequence selected from sequences SEQ ID Nos 1-16 and 17-22, preferably SEQ ID Nos 2-4, 6-8, 10-12, 14-16 and 19-22 or a fragment thereof.

29. (new) The molecule according to claim 1, wherein said therapeutic segment A has anti-tumoral activity.

30. (new) The molecule according to claim 11, wherein said therapeutic segment A is selected from the group consisting of a molecule of the family of TNF α or derivatives thereof (TRAIL-Do), a human IL4 molecule or one of its isoforms, a molecule of the family of anthracyclines or one of its active derivatives, preferably doxorubicin, a taxane molecule such as paclitaxel or docetaxel or one of its active derivatives, a methotrexate molecule or one of its active derivatives, 2-methoxyestradiol or one of its active derivatives, molecules of the family of antiprimidines such as cytosine arabinoside or difluorodesoxycytidine or one of their active derivatives, and molecules of the family of alkylating agents derived from nitrogen mustards such as phenylalanine mustard (Melphalan) or a derivative such as Chlorambucyl.

31. (new) The molecule according to claim 1, wherein said therapeutic segment A has anti-inflammatory activity.

32. (new) The molecule according to claim 13, wherein said therapeutic segment A is selected from the group consisting of an N-terminal segment of human annexin I, in particular NTA1, anti-inflammatory cytokines, and in particular IL10 and IL13 or one of their appropriate mutants, non-activating inhibitors of membranous receptors of pro-inflammatory cytokines such as in particular an inhibitor of the IL1 receptor or an appropriate mutant of this inhibitor, glucocorticoids, non-steroid anti-inflammatories or their derivatives considered to be inhibitors of cylo-oxygenase enzymes 1 and 2, and Methotrexate, and an inhibitor of the membranous receptors of the family of TNFR, in particular peptides containing at least the corresponding CRD1 extracellular domain.

33. (new) A pharmaceutical composition comprising a molecule according to claim 1.

34. (new) A method for treating a disease in a subject, wherein the method comprises administering to the subject a pharmaceutical composition according to claim 15.

35. (new) The method according to claim 16, wherein said disease is a cancer.

36. (new) The method according to claim 16, wherein said disease is an inflammatory disease.